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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,984	08/10/2001	Gary E. Harman	19603/3431 (CRF D-2716A)	5985
7590	03/22/2005		EXAMINER	
Michael L. Goldman, Esq. NIXON PEABODY LLP Clinton Square P.O. Box 31051 Rochester, NY 14603-1051			SAIDHA, TEKCHAND	
			ART UNIT	PAPER NUMBER
			1652	
DATE MAILED: 03/22/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/927,984

Applicant(s)

HARMAN ET AL.

Examiner

Tekchand Saidha

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 35-44 is/are pending in the application.
- 4a) Of the above claim(s) 1-34 and 45-54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. ***Election***

Applicants elect the invention of Group III (claims 35-44) with traverse, in their response filed February 17, 2005. Applicants' traversal is on the grounds 'that the claims of the present application are closely related and, therefore, require common areas of search and consideration. Since no benefit is derived from imposing this restriction requirement, it should be withdrawn in its entirety. '

This is not found persuasive because depending upon the restricted group (I or II or III) being examined, additional classes/subclasses have to be searched. Please see prior Office Action for details. This additional searching as explained previously would therefore involve undue burden to the Examiner. The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-34 & 45-54 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed.

3. ***Priority***

Applicant's claim for domestic priority under 35 U.S.C. 119(e), filed August 11, 2000, is acknowledged. 4.

Specification

(a) The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

(b) The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

5. ***Claim Rejections - 35 USC § 112*** (first paragraph)

Enablement

Claims 35-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of releasing (or producing) N-acetylglucosamine (or N-acetyl D-glucosamine) from a chitinous source comprising: treating a chitinous source with N-acetylhexoaminidase or β -1, 3 glucanase or endochitinase from *Trichoderma harzianum* and N-acetylhexoaminidase or β -1, 3 glucanase or endochitinase from *Streptomyces albidoflavus*, does not reasonably provide enablement for a method for producing N-acetylglucosamine employing any extra cellular inducible fungal and bacterial enzyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) [*Ex parte* Forman [230 USPQ 546 (Bd. Pat. App. & Int. 1986)]]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim. The factors most relevant to this rejection are [the scope of the claims, unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary].

The claims are drawn to encompass a method for producing N-acetylglucosamine employing any extra cellular inducible fungal and bacterial enzyme, which may or may not be any the three enzymes disclosed in the instant specification, viz., N-acetylhexoaminidase or β -1, 3 glucanase or endochitinase.

The specification provides guidance for isolating and purifying n-acetylhexoaminidase or β -1, 3 glucanase or endochitinase from *Trichoderma*

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harzianum and *Streptomyces albidoflavus*. The purified enzyme(s) individually or in combination is then used for the production of N-acetylglucosamine by degrading chitin (crab shell, for example). Specific combinations of the chitinolytic enzymes have been shown in the art to have synergistic effects in enhancing the chitinolytic properties (Lorito et al., see the abstract on paragraph 8 of this Office Action). Applicants' specification on page 35 (Table 4) shows the results of digestion on three chitin containing source material (crab, langoustino shell and colloidal chitin) with enzymes from *T. atroviride* strain P1 and *Streptomyces albidoflavus*. However, neither Table 4 nor the instant specification teach the specific type of enzyme used. Further comparing the data on Tables 2 & 4, no significant difference is noticed in the efficiency of enzymes from *T. atroviride* (Table 2) or mixture of enzymes used from *T. atroviride* strain P1 and *Streptomyces albidoflavus* (Table 4) in degrading colloidal chitin. Thus, indicating that the use of a mixture of enzymes from a fungal and a bacterial source as compared to enzyme(s) from a single source are almost comparable and the claim limitation carrying no patentable weight.

Claim 35, in its broadest interpretation, refers to a method employing a culture having fungal and bacterial cells together and which excrete the various enzymes into a medium, and the excreted enzyme are then used for releasing N-acetylglucosamine from a chitinous source. Such a culture would invariably fail because of the distinct culture conditions required for fungal and bacterial cells.

Despite knowledge in the art for isolating a variety of chitinolytic enzymes from a variety of microorganism, plants, etc., these enzymes are known to have different mode of action, employ different substrates and catalyze different end products, and therefore would lead to unpredictability in using these enzymes (extra cellular) as a catalyst for producing N-acetylglucosamine. Further, the claims would also encompass methods not

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only employing any extra cellular enzyme, but also activities that are yet to be characterized.

Thus the claims are directed to specifically encompass enormous numbers of embodiments expected to be inoperative. Since it is not routine in the art to engage in *de novo* experimentation to test for such extra cellular enzymes, where the expectation "of success is unpredictable", the skilled artisan would require additional guidance in order to make and use chitinolytic enzymes in the method for making N-acetylglucosamine, in a manner reasonably commensurate with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

6. ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless ---

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 35-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Haynes et al. [WO 97/31121, 28 August 1997]. Haynes et al. teach a method of producing N-acetylglucosamine from chitin by enzymatically hydrolyzing chitin with a combination or ensemble (or collection) of chitinolytic enzymes produced and secreted by a prokaryotic and/or eukaryotic organism. The chitinolytic enzymes can be either an endo- or exo- β -1, 4, glycanohydrolase and the chitobiase can be β -n-acetyl-glucosaminidase or β -n-acetyl-hexosaminidase (see pages 7-8). Numerous other chitinases are also described (see legends to Figures and throughout the specification). The enzyme(s) sources were bacteria, including *Streptomyces*, and fungi, including *Trichoderma*. (see page 20. Haynes et al. also teach using at least one chitinase and one chitobiase from any source (see, Claim 1), which is interpreted here as

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been derived from a bacterial and a fungal source, and therefore meet all the claim limitations, thus anticipating the claims.

7. No claim is allowed.

8. ABSTRACT ONLY

Synergistic, antifungal interactions of chitinolytic enzymes from fungi, bacteria and plants [**Lorito et al.**]

SOURCE: Chitin Enzymology, Proceedings of the International Symposium on Chitin Enzymology, 2nd, Senigallia, Italy, May 8-11, 1996 (1996), 157-164. Editor(s): Muzzarelli, Riccardo A. A. Atec Edizioni: Grottammare, Italy.

DOCUMENT TYPE: Conference, LANGUAGE: English

AB Chitinolytic enzymes with different modes of action may have synergistic activity when used in combinations. N-acetyl- β -glucosaminidases or chitin 1,4- β -chitobiosidases from fungi or bacteria were synergistic with endochitinases from fungi or plants in the inhibition of spore germination and hyphal elongation of *Botrytis cinerea* and other phytopathogenic fungi. Chitinolytic enzymes were also synergistic with other cell wall degrading enzymes (CWDEs) such as β -1,3 and β -1,6 glucanases. In addition, chitinolytic enzymes from different sources may synergistically enhance the inhibitory activity of membrane-affecting compds. (MAC). The mechanism of this interaction was investigated by monitoring the β -glucan and the chitin synthase activities associated with cell membranes. Some MACs altered structure and function of the cell membrane, inhibited the synthesis of major cell wall components in three different fungal systems (*Trichoderma*, *Botrytis* and *Saccharomyces*) and made the cell wall more sensitive to the action of chitinolytic enzymes. When MACs and enzymes were applied together against fungi, MACs could reduce the ability of the cell to repair the wall and amplify the effect of the enzymes. On the other hand, the enzyme activity, by producing a partial digestion of the cell wall, could facilitate the penetration of the MACs to reach their target at higher concns. The ability to interact with other biol. active compds. indicates that chitinolytic enzymes and genes encoding for them may be used as antimicrobial factors against chitin - containing pathogenic fungi.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571)

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272 0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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March 10, 2005